CASWELL FILE

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PC 108102

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MEMORANDUM

DATE: JUN 23 1981

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Actellic®. Meeting with ICI Americas Regarding Neurotoxicity Studies.

TOX Chem. No. 334B

FROM: Edwin R. Budd, Section Head
Toxicology Branch/HED (TS-769)

6/19/81

TO: Bev Comfort
PM Team No. 12
Registration Division (TS-767)

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

On Friday, June 5, 1981, a meeting was held with representatives from ICI Americas in the Toxicology Branch (HED) from 1:30-2:30 PM. Present at the meeting were:

Jim Wagner	ICI
David Johnstone	ICI
Bev Comfort	RD/EPA
John Doherty	TB/EPA
Ed Budd	TB/EPA

The purpose of the meeting was to discuss some problems ICI had run into in their preliminary studies preceding a 90-day neurotoxicity study they intend to carry out on chickens using Actellic® (pirimiphos-methyl). More specifically, it has been found that chickens refuse to eat diet fortified with more than about 125 ppm of Actellic® (about 6 mg/kg/day). This is considerably below the level at which they might expect to observe neurotoxic effects. How should they proceed?

EPA stated that since the purpose of this particular study is solely to evaluate the potential of Actellic® to produce neurotoxicity (other effects produced by Actellic® are of less concern in this study), the chickens would probably have to be dosed by gavage in order to administer enough test material to produce neurotoxicity. In fact, it would be essential in this study to produce neurotoxicity at least in the highest dosage level group and to establish a NOEL for the effect.

Due to the recognized difficulty in dosing so many chickens so many times by gavage, EPA would be willing to entertain modifications in the protocol for the 90-day study (which had already been submitted by ICI and commented on by EPA) to the extent that the number of birds per test group and/or the number of test groups might be decreased below the numbers originally propose by ICI. ICI agreed to submit a revised protocol incorporating such changes (as they feel appropriate) for comment by EPA.

ICI will also consider the relative dosage level at which chickens show serious cholinesterase effects (causing mortality) versus the dosage level producing neurotoxicity in their rationale for revising the protocol.

They will also discuss with the contracting laboratory the feasibility of dosing chickens by gavage in this study.

OPP:HED:TOX: E.BUDD:sb 6/18/81 X77395 Rm. 820 CM 2 #1

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Chemical:	**Pirimiphos-methyl (ANSI)**
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HED File Code	**13100 Other Tox Documents**
Memo Date:	**06/23/81**
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HED Records Reference Center
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